

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-25: (Previously Cancelled)

Claim 26: (Currently Amended) A method of synthesizing a modified therapeutic peptide capable of forming a peptidase-stabilized therapeutic peptide conjugate, the peptide comprising between 3 and 50 amino acids and having a carboxy terminal amino acid, an amino terminal amino acid, ~~a therapeutically active region of amino acids and a less therapeutically active region of amino acids~~ the method of comprising the steps of:

a) ~~if the therapeutic peptide does not contain a cysteine, then synthesizing the peptide from the carboxy terminal amino acid or the amino terminal amino acid,~~

b) sequentially and selectively oxidizing any pairs of cysteine residues in said therapeutic peptide to form disulfide bridges in said therapeutic peptide;

c) attaching a protecting group to any remaining cysteine residues that do not form said disulfide bridges in said therapeutic peptide; and

d) coupling a reactive group, ~~either directly or via a lysine,~~ to the carboxy terminal amino acid, to the amino terminal amino acid, ~~or to an amino acid,~~ or to an amino acid comprised between the carboxy terminal amino acid and the amino terminal amino acid, wherein the reactive group is capable of reacting with amino groups, hydroxyl groups or thiol groups on blood component to form a covalent bond therewith;

b) ~~if the therapeutic peptide contains only one cysteine, then synthesizing the peptide in accordance with step a) while providing the cysteine in a protected form, the~~

cysteine remaining protected prior to and after coupling, either directly or via a lysine, of the reactive group to the peptide;

e) — if the therapeutic peptide contains two cysteines, synthesizing the peptide in accordance with step a), and either

i) — cleaving the peptide from the resin, oxidizing the two cysteines cysteines to form a disulfide bridge, and coupling the reactive group to the peptide, either directly or via a lysine; or

ii) — oxidizing the two cysteines to form the disulfide bridge, coupling the reactive group to the peptide, and cleaving the modified therapeutic peptide from the resin; or

iii) — coupling the reactive group to the peptide, either directly or via a lysine, cleaving the peptide from the resin, and oxidizing the two cysteines to form the disulfide bridge; or

iv) — coupling the reactive group to the peptide, either directly or via a lysine, oxidizing the two cysteines to form the disulfide bridge, and cleaving the modified peptide from the resin;

d) — if the therapeutic peptide contains more than two cysteines, synthesizing the peptide in accordance with step a), optionally cleaving the peptide from the resin, sequentially and selectively oxidizing each pair of cysteines to form disulfide bridges, and, if the number of cysteines is odd, protecting the last cysteine remaining, and

i) — if cleaved from the resin, purifying the peptide prior to the

~~coupling of the reactive group, either directly or via a lysine, to the peptide;~~

~~if not cleaved from the resin, cleaving and purifying the peptide prior to
the coupling of the reactive group, either directly or via a lysine, to the peptide.~~

Claim 27: (Currently Amended) A method as claimed in claim 26 ~~27~~ wherein the reactive group is selected from the group consisting of succinimidyl- and maleimido-containing groups.

Claim 28: (Cancelled)

Claim 29: (Currently Amended) A method as claimed in claim 27 ~~28~~ wherein the reactive entity is a maleimido-containing group.

Claim 30: (Currently Amended) A method as claimed in claim 26 ~~27~~, further comprising bonding a lysine residue to said peptide, wherein the reactive group is coupled to the peptide via a said lysine residue.

Claim 31: (Currently Amended) A method as claimed in claim 26 ~~27~~ wherein the reactive group is coupled to the carboxy terminal amino acid of the peptide.

Claim 32: (Currently Amended) A method as claimed in claim 26 ~~27~~ wherein the peptide does not contain a cysteine.

Claim 33: (Currently Amended) A method as claimed in claim 26 ~~27~~ wherein the therapeutic peptide contains two cysteines ~~and the peptide is cleaved from the resin~~, the two cysteines are oxidized to form a disulfide bridge, and the reactive group is coupled to the peptide, ~~either directly or via a lysine~~.

Claim 34: (Currently Amended) A method as claimed in claim 32 ~~33~~ wherein the peptide is synthesized from the carboxy terminal amino acid.

Claim 35: (Currently Amended) A method of synthesizing a modified therapeutic peptide and ~~capable of~~ forming a peptidase-stabilized therapeutic peptide conjugate, the peptide comprising between 3 and 50 amino acids and having a carboxy terminal amino acid, and an amino terminal amino acid, ~~a therapeutically active region of amino acids and a less therapeutically active region of amino acids, the peptide not containing a~~ cysteine, the method comprising the steps of

synthesizing the peptide from the carboxy terminal amino acid, and

coupling a maleimido-containing group, ~~either directly or via a lysine,~~ to the carboxy terminal amino acid, ~~to the amino terminal amino acid, or to an~~ amino acid ~~comprised between the carboxy terminal amino acid and the amino terminal amino acid,~~ and

reacting the maleimido-containing group ~~reacting with a thiol group groups on a~~ blood component to form a covalent bond therewith.

Claim 36: (Currently Amended) A method as claimed in claim 35 ~~36~~ wherein the maleimido-containing group is coupled to the carboxy terminal amino acid.

Claim 37: (Currently Amended) A method as claimed in claim 35 ~~36~~, further comprising bonding a lysine residue to said peptide, wherein the maleimido-containing group is coupled to the peptide via said lysine residue ~~a lysine~~.